IN THE SPECIFICATION

Amend the specification as follows.

Delete the paragraph on page 20, spanning lines 4-33, of the specification and insert the following therefor:

NAT1 (N-acetyltransferase 1) and NAT2 (N-acetyltransferase 2) also activate PAH and heterocyclic amines (HAA). The enzymes catalyse N-acetylation, O-acetylation, and N,O-acetylation. The O-acetylation reaction is considered the most risky, with the potential for forming chemical carcinogens that can bind to DNA. The N-acetylation reaction can occur on a compound after a P450 has inserted an oxygen, thus increasing the water solubility of the compound so it may be excreted. Due to this activity, the NAT genes are often considered as both Phase I and Phase II type enzymes. The literature describing a cancer link focuses on the activation activity of the enzymes, so they will be listed in the Phase I section only. There are 3 separate N-acetyltransferase genes in humans, two are active genes: NAT1 and NAT2, and a pseudogene, NATP. Pseudogenes have the same sequence, but lack apparent function and promoter elements and are not expressed in cells (i.e. the gene is not transcribed into RNA then translated into amino acids to make a protein/enzyme) (Perera, 2000). NAT1 and NAT2 genes are located on chromosome 8 at 8p21.3-21.1, both genes are 870 bp long and both code for a protein 290 amino acids in length. The genes are highly polymorphic and epidemiological studies have sometimes given conflicting information regarding links with cancer. The genes show geographical and ethnic variation and the enzyme activity varies considerably within different tissues or organs. There are approximately 20 polymorphisms for NAT1 known to date, but the

list below only includes the polymorphisms that have shown a link to cancer (Hein, 2000a). The current list of nomenclature and polymorphisms is kept at a web site:

~~http://www.louisville.edu/medschool/pharmacology/NAT.html~~

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